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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/805,816	03/13/2001	Mohammad A. Heidaran	07078-030001	6205

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EXAMINER
DI NOLA BARON, LILIANA

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 03/12/2003

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/805,816	HEIDARAN ET AL.	
	Examiner	Art Unit	
	Liliana Di Nola-Baron	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☒ Claim(s) *7,9 and 11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

Receipt of Applicant's amendment, filed on January 10, 2003, is acknowledged.

Claim Objections

1. Claims 7, 9 and 11 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 7, 9 and 11 read on a method according to claims 20, 21, 22 or 23, thus failing to further limit the subject matter of a previous claim.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

3. Claims 1- 23 are rejected under 35 U.S.C. 102(e) as being anticipated by Heidaran et al.

Heidaran et al. discloses collagen-polysaccharide matrices, and preferably collagen-hyaluronic acid matrices containing BMPs and GDFs for the treatment of bone tumors and teaches that the collagen used in the invention is Type I or Type II collagen (See cols.1-2). Heidaran et al.

teaches that the invention is based upon the findings that a collagen-polysaccharide matrix containing TGF-β, which includes BMPs and GDFs, inhibits growth of osteosarcoma, but elicits opposite response in normal osteoblasts versus tumor cells, and defines "repair" as growth of new tissue (See col. 1, line 63 to col. 2, line 60). Heidaran et al. teaches that the matrices can be used in vitro and in vivo and can be administered by implantation, direct application or injection (See col. 6, lines 62-67).

The compositions and their medical applications provided by Heidaran et al. meet the limitations of claims 1-23 of the instant application, as they contemplate compositions comprising a collagen-hyaluronate matrix comprising BMPs and GDFs and methods comprising exposing the cells to said compositions. Thus, Heidaran et al. anticipates the claimed invention.

4. Claims 1-4 and 12-15 are rejected under 35 U.S.C. 102(e) as being anticipated by Hattersley et al. (U.S. Patent 5,902,785).

Hattersley et al. provides compositions for the induction of cartilaginous tissue formation and tissue repair, comprising BMP-4 (See cols. 1-2), and a matrix comprising collagen and a sequestering agent, such as hyaluronic acid (See col. 7, line 51 to col. 8, line 65). Hattersley et al. teaches that the BMP-12 related subfamily of proteins was shown to induce tendon/ligament-like tissue formation and repair (See cols. 1-2). In particular, Hattersley et al. teaches that a composition comprising BMP-4 in combination with other BMPs may be especially useful for the treatment of articular cartilage (See col. 2, lines 39-51).

The compositions disclosed by Hattersley et al. and their use meet the limitations of claims 1-4 and 12-15 of the instant application, as they contemplate compositions comprising collagen and BMP-4 or collagen, BMP-4 and hyaluronate, and methods comprising exposing cells to said compositions. Thus, Hattersley et al. anticipates the claimed invention.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 12-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. (U.S. Patent 5,118,667).

Adams et al. provides pharmaceutical compositions comprising a bone growth factor, such as TGF-β (which includes GDFs) and BMP (See col. 3, lines 26-38). Adams et al. teaches that the compositions may be implanted at the site in a sustained-release carrier, which includes collagen matrices (See col. 7, lines 7-24), the composition of the invention can be coated on implant devices and the viscosity of the coating solution can be increased by adding hyaluronate (See col. 7, lines 40-58).

Thus, Adams et al. provides pharmaceutical compositions, as claimed in the instant application. Adams et al. does not specifically teach that the amount of BMP-4 is sufficient to induce or enhance chondrogenesis, however, the compositions of the prior art comprise an osteogenically effective amount of the bone growth factor, and the reference teaches that an osteogenically

effective dose is also "pharmaceutically effective" (See col. 5, lines 14-62). The burden is shifted to Applicant to show that the pharmaceutically effective amount of BMP-4 disclosed by the prior art would not be capable of inducing chondrogenesis, as claimed in the instant application.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to apply the teachings of Adams et al. to device compositions comprising bone growth factors in carrier matrices. The expected result would have been successful compositions. Because of the teachings of Adams et al., that compositions may comprise bone growth factors in a collagen matrix comprising hyaluronate, one of ordinary skill in the art would have a reasonable expectation that the compositions claimed in the instant application would be successful. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

7. Applicant's arguments filed on January 10, 2003 have been fully considered but they have been found only partially persuasive.

8. Applicant argues that the methods and compositions disclosed by Heidaran et al. are directed to the treatment of bone tumors, and the tumor cells are not enhanced or induced by the compositions and methods of the invention, but rather inhibited. In response to said argument, it is noted that Heidaran et al. teaches that the invention is based upon the findings that a collagen-polysaccharide matrix containing TGF-β, which includes BMPs and GDFs, inhibits growth of osteosarcoma, but elicits opposite response in normal osteoblasts versus tumor cells, and defines

"repair" as growth of new tissue (See col. 1, line 63 to col. 2, line 60). Thus, the compositions and methods disclosed by the prior art induce formation of normal tissue.

9. In response to Applicant's argument, that Hattersley et al. requires the presence of at least two active substances, whereas Applicant claims methods and compositions comprising only BMP-4, it is noted that the "comprising" language of claims 1-4 and 12-15 allows for the presence of additional active factors in the compositions and methods disclosed by the prior art.

10. Applicant argues that the methods and compositions disclosed by Adams et al. are directed to the stimulation of new bone formation, and the reference does not teach induction or enhancement of chondrogenesis. This argument has been found persuasive with respect to claims 1-11 of the instant application, since claims 1-11 are directed to methods for inducing or enhancing chondrogenesis. The prior art, however, is still applicable to claims 12-19 of the instant application, since said claims are directed to compositions comprising a matrix containing BMP-4, and intended use has no patentable weight in composition claims. Adams et al. does not specifically teach that the amount of BMP-4 is sufficient to induce or enhance choondrogenesis, however, the compositions of the prior art comprise an osteogenically effective amount of the bone growth factor, and the reference teaches that an osteogenically effective dose is also "pharmaceutically effective" (See col. 5, lines 14-62). The burden is shifted to Applicant to show that the pharmaceutically effective amount of BMP-4 disclosed by the prior art would not be capable of inducing chondrogenesis, as claimed in the instant application.

Conclusion

11. Claims 1-23 are rejected.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liliana Di Nola-Baron whose telephone number is 703-308-8318. The examiner can normally be reached on Monday through Thursday, 5:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the

organization where this application or proceeding is assigned are 703-305-3592 for regular communications and 703-305-3592 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 308-1234/ 1235.

SKM

February 25, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600